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## Data Article

# Exogenous control over intracellular acidification: Enhancement via proton caged compounds coupled to gold nanoparticles and an alternative pathway with DMSO



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## ARTICLE INFO

## Article history:

Received 8 September 2015

Received in revised form

22 November 2015

Accepted 11 December 2015

Available online 21 January 2016

## Keywords:

Proton caged compounds

DMSO

Intracellular proton release

## ABSTRACT

Proton caged compounds exhibit a characteristic behavior when directly dosed into cells or being coupled to gold nanoparticles prior to the dosing. When irradiated in the near ultraviolet region, they release protons that interact with intracellular  $\text{HCO}_3^-$  to yield  $\text{H}_2\text{CO}_3$ . The dissociation of carbonic acid, then, releases  $\text{CO}_2$  that can be distinctively singled out in infrared spectra.

In the process of searching a pathway to augment the intracellular uptake of proton caged compounds, we probed the association of 1-(2-nitrophenyl)-ethylhexadecyl sulfonate (HDNS) with DMSO, an agent to enhance the membrane permeability. We found out a different UV-induced protonation mechanism that opens up

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<http://dx.doi.org/10.1016/j.dib.2015.12.032>

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to new conduits of employing of proton caged compounds. Here, we report the infrared data we collected in this set of experiments.  
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Specifications Table

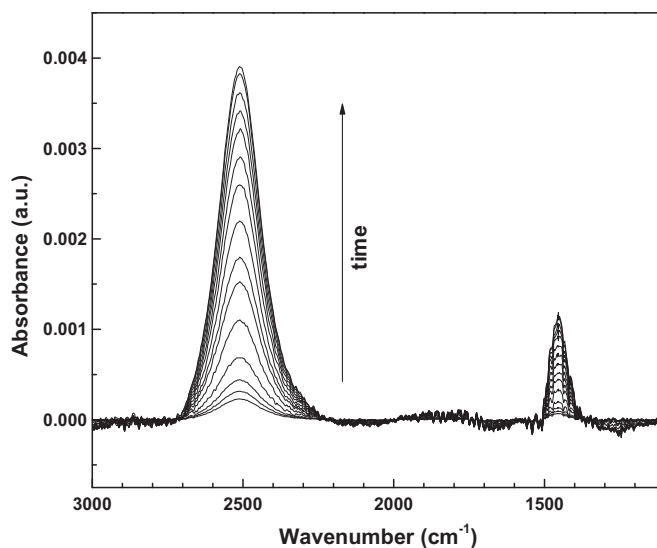
Subject area	<b>Biochemistry, Genetics and Molecular Biology</b>
More specific sub- ject area	Photochemistry, Photobiology
Type of data	Figures and Graphs
How data was acquired	Infrared spectroscopy, Bruker IFS66/VS interferometer, ultraviolet irradiation by deuterium discharge lamp (Acton Research Corporation) equipped with a band-pass FGUV11 filter (Thorlabs)
Data format	Raw and analyzed data
Experimental factors	NIH-3T3 cells are dosed with the proton caged compound HDNS and with DMSO to enhance the cells permeability
Experimental features	Infrared spectra are collected from NIH-3T3 cells upon irradiation with near UV-light and compared spectra of cells where the vectorization is achieved with gold nanoparticles
Data source location	Rome, Italy, 41.8536°N, 12.6033°E and 41.9033°N, 12.5158°E
Data accessibility	Data are with this article

Value of the data

- These data exhibit the behavior of a proton caged compound into 3T3-NIH cells when dosed in association with the membrane cell permeability enhancer DMSO.
- The infrared spectra of the cells are taken after filtered ultraviolet light irradiation and show characteristic band variations.
- The band variation is different than in absence of DMSO, also compared to the vectorization with gold nanoparticles, opening up to new pathways of employing proton caged compounds.

1. Data

The first experiment to probe proton caged compounds (PCCs) as tools to manipulate and monitor the intracellular pH was performed by dosing the 1-(2-nitrophenyl)-ethylhexadecyl sulfonate (HDNS) to 3T3-NIH cells [1] and observing the effects on a single cell. PCCs yield one proton per molecule, therefore the intracellular proton release is related to the amount of PCCs that can be conveyed into the cells. An enhanced uptake can be obtained by vectorization of PCCs with gold nanoparticles (AuNPs) [2], or intervening on the cellular permeability, for instance, with DMSO. We have explored both pathways, the experiments with DMSO being antecedent the ones with AuNPs, because they do not require ad hoc synthesis of sulfur functionalized PCCs [3]. The outcome, though not straightforwardly applicable in the intracellular pH manipulation, is still quite interesting. Therefore, we report here the data we collected.

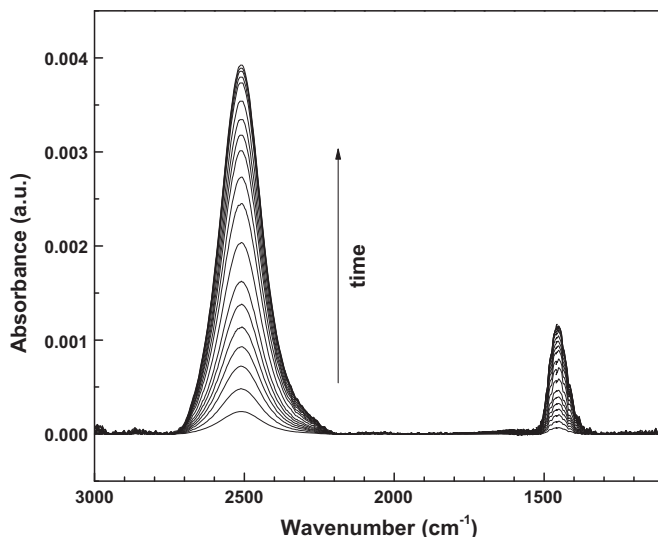


**Fig. 1.** Infrared absorption spectra after irradiation of NIH-3T3 cells dosed with HDNS and DMSO: first data set. The arrow indicates the spectra evolution as a function of time.

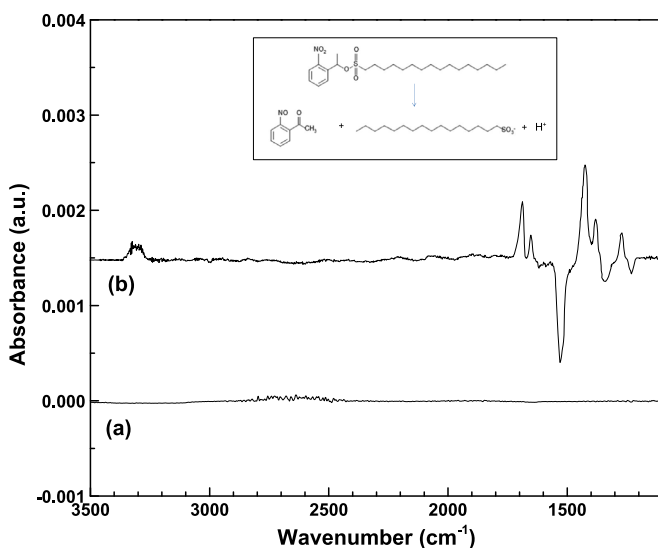
## 2. Experimental design, materials and methods

The effects of the DMSO on the intracellular uptake of HDNS were monitored by dosing them simultaneously to 3T3-NIH cells and subsequently probing them by infrared spectroscopy upon irradiation with UV-light. More in detail, NIH 3T3 Swiss Albino Mouse Fibroblast cells (ECACC Catalog number 85022108) were cultured directly on UV-transparent CaF<sub>2</sub> windows in Dulbecco's Modified Eagle Medium (DMEM) with HCO<sub>3</sub><sup>−</sup> (3.7 g/L) and supplemented with 10% fetal bovine serum up to full coverage. Afterwards, the cells were incubated with 3 mg HDNS and 2  $\mu$ L DMSO in 3 mL in DMEM for 1 h. The amount of DMSO was chosen as the minimum amount to allow an increased membrane permeability [4,5]. Afterwards the cell-coated window was transferred to the sample holder for liquids for collecting the infrared spectra, using a 12  $\mu$ m Mylar spacer. The experimental setup was the same as the one used afterwards for the gold coupled PCCs [3] (a Bruker IFS66/VS interferometer, in transmission mode with a resolution of 2 cm<sup>−1</sup>). Infrared spectra were collected in the 3500–1000 cm<sup>−1</sup> range for reference spectra and 3000–1000 cm<sup>−1</sup> range for the cells. A few sequential infrared spectra of the cells were taken to verify their stability. Afterwards the samples were irradiated once for 1 min with near-UV light, by using a deuterium discharge lamp (Acton Research Corporation) equipped with a band-pass FGV11 filter (Thorlabs) in the 275–375 nm. A few independent measurements were performed and they all provide similar outcome. Here we report two of them in Figs. 1 and 2. The data are treated with the OPUS software for vector normalization and offset correction. Finally, they are normalized by the first spectrum after irradiation and exported as ASCII files. The spectra are taken at intervals of 2 min. Therefore, the whole datasets are taken in a time span of 30 (1st set) to 40 min (2nd set). In the second data set a saturation level may be appreciated.

The datasets are characterized by the arising of two bands which grow upon irradiation, one, rather large, centered at 2510 cm<sup>−1</sup> and the other one narrower centered at 1452 cm<sup>−1</sup>. No contribution is found, instead, at 2343 cm<sup>−1</sup> the typical value for the intracellular CO<sub>2</sub>. The data, however, are largely reproducible, and are not related to dead cells, since we had previously verified that in our experimental set up they do not provide any spectral variation as a function of irradiation and of time. Furthermore, we made checks to identify the new arising features, by comparing them to those of DMSO and HDNS in DMSO upon irradiation. In Fig. 3 the difference spectra are reported of DMSO (panel (a)) and HDNS M in DMSO (panel (b)) before and 5 min after UV irradiation. It can be observed that that DMSO is not affected by the irradiation. The PCC is obviously responsive to the irradiation



**Fig. 2.** Infrared absorption spectra after irradiation of NIH-3T3 cells dosed with HDNS and DMSO: second data set. The arrow indicates the spectra evolution as a function of time.



**Fig. 3.** Infrared difference spectra before and after UV-irradiation: (a) DMSO, (b) HDNS in DMSO. The HDNS photo-decomposition mechanism is shown in the inset.

and shows a number of positive and negative peaks that correspond to the breaking of the HDNS ester bond and the formation of a ketone and a sulfonic moiety, according to the mechanism illustrated in the inset of Fig. 3. In particular, the negative peaks at  $1527\text{ cm}^{-1}$  and  $1346\text{ cm}^{-1}$  are associated to the asymmetric and symmetric stretching of the  $\text{NO}_2^-$  group, the negative peak at  $1235\text{ cm}^{-1}$ , to the sulfonic group. The positive peak at  $1691\text{ cm}^{-1}$  can be associated to the newly formed ketone, whereas the peaks at  $1424\text{ cm}^{-1}$ ,  $1378\text{ cm}^{-1}$  and  $1271\text{ cm}^{-1}$  are related to the cis and trans NO stretching [6]. The protons released in DMSO give rise to two new bands at  $1652\text{ cm}^{-1}$  and  $3320\text{ cm}^{-1}$  which can be associated to the bending and stretching of newly formed  $\text{O-H}^+$

interactions, as already observed for DMSO protonation by HCl [7]. The region around  $2500\text{ cm}^{-1}$  is free both for DMSO and for HDNS in DMSO. This rules out that in the datasets of the cells, the increase of features intensity upon irradiation is the direct observation of processes solely related to the molecules themselves. The interpretation is therefore to be found in processes which may affect the cells as effect of the proton release. There are many possible intracellular contributions to the feature at  $1452\text{ cm}^{-1}$ , such as side chains and protonated side chains of several aminoacids and proteins as well as the Amide II band [8,9].

The band at  $2510\text{ cm}^{-1}$  is rarely observed. The most likely contributions can be associated to the dimer form of carboxylic acids, such as in solid state formic acid [10]. Furthermore, bands at  $\sim 2500\text{ cm}^{-1}$  are observed also for saturated carboxylic dimers [11]. This gives an indication of a direct protonation of aminoacids and proteins, rather than the reaction with  $\text{HCO}_3^-$ , when DMSO is used is association to a PCC. Alternatively, the band at  $2510\text{ cm}^{-1}$  may be associated to processes which produce CSO [12] or SH [13].

However, in general, the arising of the features at  $2510\text{ cm}^{-1}$  and  $1452\text{ cm}^{-1}$  mainly points at a protonation mechanism induced by PCC and DMSO which affects the intracellular components in a more extended way as compared to the PCC/AuNPs or the PCC alone.

## Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at <http://dx.doi.org/10.1016/j.dib.2015.12.032>.

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